# **WEST Search History**

Hide Items Restore Clear Cancel

DATE: Monday, November 29, 2004

Hide?	Set Nam	<u>e Query</u>	Hit Count
	DB=US	PT; PLUR=YES; OP=ADJ	
	L24	E6 and HPV 18.clm.	27
	L23	E6 and HPV 16.clm.	45
	L22	E6 and HPV 16	310
	L21	E6 and HPV 18	165
	DB=DV	VPI; PLUR=YES; OP=ADJ	
	L20	E6 and HPV 18	10
	L19	E6 and HPV 16	24
	DB=US	PT; PLUR=YES; OP=ADJ	
	L18	US-6010704-A.did.	1
	L17	US-6010704-A.did.	1
	L16	US-5919615-A.did.	1
	L15	US-5919615-A.did.	1
	DB = DV	VPI; PLUR=YES; OP=ADJ	
	L14	Breitburd.in.	3
	DB=EP	AB; PLUR=YES; OP=ADJ	
	L13	WO-2004005469-A2.did.	1
	L12	WO-2004005469-A2.did.	1.
	DB=DV	VPI; PLUR=YES; OP=ADJ	
	L11	HU Y X.in.	3
	DB=US	PT; PLUR=YES; OP=ADJ	
	L10	HU.in. and papillomavirus	5
	L9	HU.in. and virus	120
	L8	HU.in.	2131
	L7	4777239.pn.	1
	L6	6743593.pn.	1
	L5	5679509.pn. and antibody	1
	L4	5679509.pn.	1
	L3	L1 and 2	1
	L2	L1 and 24	1
	L1	6783763.pn.	1

END OF SEARCH HISTORY

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Middle Aged
      Oncogene Proteins, Viral: BI, biosynthesis
     *Papillomavirus, Human: IP, isolation & purification
     *Papovaviridae Infections
     *Tumor Virus Infections
     0 (Antibodies, Viral); 0 (DNA, Viral); 0 (E6 protein,
     Human papillomavirus type 16); 0 (Oncogene Proteins, Viral)
     ANSWER 4 OF 11
                        MEDLINE on STN
L9
AN
     96377304
                  MEDLINE
     PubMed ID: 8783151
DN
     Detection of human papillomavirus type-16 DNA utilising microtitre-plate
TI
     based amplification reactions and a solid-phase enzyme-immunoassay
     detection system.
ΑU
     Cavuslu S; Starkey W G; Kaye J N; Biswas C; Mant C; Kell B; Rice P; Best J
     M; Cason J
CS
     Richard Dimbleby Laboratory of Cancer Virology, Department of Virology,
     Rayne Institute, United Medical School, St Thomas' Hospital, London, UK.
SO
     Journal of virological methods, (1996 Apr 26) 58 (1-2) 59-69.
     Journal code: 8005839. ISSN: 0166-0934.
CY
     Netherlands
DT
     Journal; Article; (JOURNAL ARTICLE)
     English
LΑ
FS
     Priority Journals
EM
     199612
ED
     Entered STN: 19970128
     Last Updated on STN: 19970128
     Entered Medline: 19961205
AΒ
     The development of a nested polymerase chain reaction (PCR) assay to
     detect low concentrations of human papillomavirus type-16 (
     HPV-16) DNA for epidemiological studies is described.
     The PCR utilises primers located in the E5 open reading frame, has an
     analytical sensitivity of 4 HPV-16 genomes and does
     not produce amplicons from other common genital HPVs (types-6, -11, -18,
     -31 and 33). This assay was carried out in 96-well plates utilising
     internal primers labelled with dinitrophenol (DNP) and biotin so that
     amplicons can be captured onto streptavidincoated plates and detected
     using an alkaline phosphatase-labelled monoclonal antibody to
     DNP. The assay was effective for detecting HPV-16 DNA
     in plasmids, cell-lines and, both freshly collected or archival
     (formalin-fixed/paraffin embedded) clinical specimens. This system is
     therefore suitable for epidemiological studies to identify individuals
     infected with HPV-16 DNA in episomal form who may be
     at increased risk of developing anogenital carcinomas.
     Check Tags: Female; Human; Support, Non-U.S. Gov't
     Cervical Intraepithelial Neoplasia: PA, pathology
     *Cervical Intraepithelial Neoplasia: VI, virology
     Cervix Neoplasms: PA, pathology
     *Cervix Neoplasms: VI, virology
      DNA Primers
     *DNA, Viral: AN, analysis
      Evaluation Studies
     Hela Cells
     *Immunoenzyme Techniques
     *Oncogene Proteins, Viral: GE, genetics
     Papillomavirus, Human: GE, genetics
     *Papillomavirus, Human: IP, isolation & purification
     *Polymerase Chain Reaction: MT, methods
     Sensitivity and Specificity
     Tumor Cells, Cultured
CN
    0 (DNA Primers); 0 (DNA, Viral); 0 (E6 protein, Human
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\*Esophageal Neoplasms: VI, virology

papillomavirus type 16); 0 (Oncogene Proteins, Viral); 0 (oncogene protein E5, human papillomavirus type 16); 0 (oncogene protein E7, human papillomavirus type 16) ANSWER 5 OF 11 MEDLINE on STN 96098816 MEDLINE PubMed ID: 8533490 [Interferon-alpha controls HPV infection in cervix epithelium]. Interferon-alpha kontrolliert die HPV-Infektion im Zervixepithel. Labeit D; Labeit S; Berger M; Gallati H; Rosenberg R; Friese K Universitatsfrauenklinik Mannheim. Zentralblatt fur Gynakologie, (1995) 117 (11) 566-77. Journal code: 21820100R. ISSN: 0044-4197. GERMANY: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE) German Priority Journals; AIDS 199601 Entered STN: 19960220 Last Updated on STN: 19960220 Entered Medline: 19960129 Decreased immune response is necessary for a prolonged HPV-infection and allows HPV to be virulent as an oncogene. This study shows that HPV-infection in cervical epithelium is determined by the immune system and IFN-alpha can be shown to be a prognostic parameter for the HPV-infection. The cytokines (IFN-alpha, IFN-gamma, and TNF-alpha) from stimulated peripheral blood mononuclear cells (PBMC) were measured using monoclonal IFN-antibodies and ELISA test. To detect HPV-16, PCR (e6 and e7 areas) was used, followed by southern-blot of the PCR-products. In all of our patients (n = 139) no cytological change was observed in the cervical epithelium over a period of 3 years. Comparison was made between 3 groups: 1: controls (n = 89, HPV-pos. n = 6) 2: registered prostitutes without drug abuse (n = 30, HPV-pos. n = 6) and 3: HIV-infected, previous drug users (CDC II, n = 6) 20, HPV-pos. n = 2). RESULTS: The stimulated IFN-alpha values are highest in the control collective (169 +/- 35 U/ml) and are significantly lower in the prostitutes (98 +/- 26 U/ml, p < 0.05) and in the HIV-infected group (49 +/- 15 U/ml, p < 0.01). The difference between the latter groups being significant as well (p < 0.05). Dividing the controls into HPV-16 positive and HPV-16 negative subgroups, the IFN-alpha values are significantly higher in HPV-16 negative group (193 +/- 48 U/ml) compared to HPV-16 positive group (38  $\pm$  4 3 U/ml, p < 0.05). Also in the collective of prostitutes and HIV infected patients there is a similar significant difference between the HPV-16 positive and HPV-16 negative patients (Prostitutes: HPV-16 negative = 94 +/- 21 U/ml, HPV-16 positive = 36 + /- 7 U/ml, p < 0.05; HIV-infected: **HPV-16** negative = 35 + /- 13 U/ml, HPV-16 positive = 13 + /- 3U/ml). Check Tags: Female; Human; Support, Non-U.S. Gov't AIDS-Related Opportunistic Infections: IM, immunology \*Antiviral Agents: BL, blood \*Cervix Neoplasms: IM, immunology Cervix Uteri: VI, virology English Abstract Interferon Type II: BL, blood \*Interferon-alpha: BL, blood

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\*Papillomavirus, Human: IM, immunology
\*Papovaviridae Infections: IM, immunology

Prostitution Tumor Necrosis Factor: ME, metabolism \*Tumor Virus Infections: IM, immunology RN82115-62-6 (Interferon Type II) CN 0 (Antiviral Agents); 0 (Interferon-alpha); 0 (Tumor Necrosis Factor) Ь9 ANSWER 6 OF 11 MEDLINE on STN 95114033 ANMEDLINE DN PubMed ID: 7529250 TIComparison of peptide enzyme-linked immunosorbent assay and radioimmunoprecipitation assay with in vitro-translated proteins for detection of serum antibodies to human papillomavirus type 16 E6 and E7 proteins. Sun Y; Shah K V; Muller M; Munoz N; Bosch X F; Viscidi R P AU Department of Immunology and Infectious Diseases, Johns Hopkins University CS School of Hygiene and Public Health, Baltimore, Maryland 21205. NC RO1-CA56514 (NCI) Journal of clinical microbiology, (1994 Sep) 32 (9) 2216-20. SO Journal code: 7505564. ISSN: 0095-1137. CY United States Journal; Article; (JOURNAL ARTICLE) DT(MULTICENTER STUDY) LΑ English Priority Journals FS 199502 EM Entered STN: 19950217 ED Last Updated on STN: 19960129 Entered Medline: 19950206 AΒ Antibodies to human papilloma virus (HPV) type 16 (HPV -16) E6 and E7 proteins in serum are markers for HPV-associated invasive cervical carcinoma. We compared two assays, a radioimmunoprecipitation assay with in vitro-translated HPV-16 E6 and E7 proteins and an enzyme-linked immunosorbent assay (ELISA) with E6 and E7 synthetic peptides, for their abilities to discriminate serologically between patients with invasive cervical cancer and controls. Among the patients, antibody prevalences were higher by the E6 radioimmunoprecipitation assay (55.7%) than by the **E6** peptide ELISA (15.5%), but among the controls, they were lower by the radioimmunoprecipitation assay (1.7%) than by the E6 peptide ELISA (5%). For E7, antibody prevalences among the patients were comparable by the radioimmunoprecipitation assay (43%) and the peptide ELISA (41%), but

between patients with invasive cervical cancer and controls and that this is related to the ability of the radioimmunoprecipitation assay to detect conformational epitopes.

CT Check Tags: Comparative Study; Female; Human; Support, U.S. Gov't, P.H.S. \*Antibodies, Viral: BL, blood

of reactivity to the **E6** protein and a marked decrease in reactivity to the E7 protein. Our study showed that the

among the controls they were higher by the E7 peptide ELISA (17.4%) than by the radioimmunoprecipitation assay (4.1%). There was good agreement between the E7 radioimmunoprecipitation assay and the E7 peptide ELISA among patients but not among controls. In tests with representative sera, heat denaturation of the translated proteins resulted in a complete loss

radioimmunoprecipitation assay discriminates better than the peptide ELISA

\*Antigens, Viral: IM, immunology Carcinoma: PA, pathology

Antibodies, Viral: IM, immunology

Carcinoma: PA, pathology Carcinoma: VI, virology Case-Control Studies

Cervix Neoplasms: PA, pathology Cervix Neoplasms: VI, virology

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Colombia
     *Enzyme-Linked Immunosorbent Assay
      Epitopes: CH, chemistry
     *Epitopes: IM, immunology
     Heat
     Neoplasm Invasiveness
     *Oncogene Proteins, Viral: IM, immunology
     *Papillomavirus, Human: IM, immunology
      Papillomavirus, Human: IP, isolation & purification
     *Papovaviridae Infections: BL, blood
      Papovaviridae Infections: IM, immunology
      Peptide Fragments: CS, chemical synthesis
     *Peptide Fragments: IM, immunology
     *Precipitin Tests
      Protein Conformation
      Protein Denaturation
     *Radioimmunoassay
     *Recombinant Fusion Proteins: IM, immunology
      Sensitivity and Specificity
      Translation, Genetic
     *Tumor Virus Infections: BL, blood
     Tumor Virus Infections: VI, virology
     0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (E6
CN
     protein, Human papillomavirus type 16); 0 (Epitopes); 0 (Oncogene
     Proteins, Viral); 0 (Peptide Fragments); 0 (Recombinant Fusion Proteins);
     0 (oncogene protein E7, human papillomavirus type 16)
Ь9
    ANSWER 7 OF 11
                        MEDLINE on STN
ΑN
     94064167
                 MEDLINE
DN
     PubMed ID: 8244575
     Serologic response in human papillomavirus-associated invasive cervical
TΙ
     cancer.
ΑU
    Viscidi R P; Sun Y; Tsuzaki B; Bosch F X; Munoz N; Shah K V
     Eudowood Division of Infectious Disease, Department of Pediatrics, Johns
CS
     Hopkins University School of Medicine, Baltimore, MD.
NC
     R01-CA56514 (NCI)
SO
     International journal of cancer. Journal international du cancer, (1993
    Nov 11) 55 (5) 780-4.
     Journal code: 0042124. ISSN: 0020-7136.
CY
    United States
DT
     Journal; Article; (JOURNAL ARTICLE)
LΑ
     English
FS
     Priority Journals
ĒΜ
     199312
    Entered STN: 19940201
ED
     Last Updated on STN: 19940201
     Entered Medline: 19931223
     Human papillomavirus (HPV) transforming proteins E6 and E7 are
AΒ
     uniformly expressed in HPV-associated cervical cancer. Our objective was
     to measure antibodies to HPV-16 E6
     and E7 proteins in cervical cancer patients using an assay which would
     detect antibodies to conformational epitopes. Serum
     specimens obtained from two case-control studies of HPVs and cervical
     cancer were tested. The studies were performed in Cali, Colombia, South
    America and in 9 provinces of Spain. Cases consisted of women with
     invasive cervical cancer associated with HPV-16 or
     other HPV types and women with HPV-16-associated
    high-grade cervical intra-epithelial neoplasia (CIN-3). Controls for
     invasive cases and CIN-3 cases were women who had no cytologic
     abnormalities and who were matched for age and country of residence.
     Serum antibodies to HPV-16 E6 and
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E7 proteins were detected by radio-immunoprecipitation of in vitro translated proteins. Antibodies to the E6 and E7 protein were observed among 56% and 43%, respectively, of invasive cases and 1.7% and 4.1%, respectively, of controls. Antibodies to either protein were detected in 72% of sera from invasive cases and 5.8% of sera from controls. High antibody reactivity and antibodies to both proteins were found almost exclusively in invasive cases. The frequency of antibodies to the E6 protein and the E7 protein among CIN-3 cases did not differ significantly from the CIN-3 controls. Five women with HPV-18-associated invasive cervical cancer were negative for serum antibody to HPV -16 E6 and E7 proteins. Antibodies to HPV-16 E6 and E7 proteins appear to be partially virus-specific and disease state-specific markers of HPV-associated cervical cancer. Check Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S. \*Antibodies, Viral: BL, blood Case-Control Studies \*Cervical Intraepithelial Neoplasia: IM, immunology \*Cervical Intraepithelial Neoplasia: MI, microbiology \*Cervix Neoplasms: IM, immunology \*Cervix Neoplasms: MI, microbiology Colombia Immunosorbent Techniques Oncogene Proteins, Viral: IM, immunology \*Papillomavirus, Human Spain 0 (Antibodies, Viral); 0 (E6 protein, Human papillomavirus type 16); 0 (Oncogene Proteins, Viral); 0 (oncogene protein E7, human papillomavirus type 16) ANSWER 8 OF 11 MEDLINE on STN 93170933 MEDLINE PubMed ID: 8382193 Serological response to HPV 16 in cervical dysplasia and neoplasia: correlation of antibodies to E6 with cervical cancer. Ghosh A K; Smith N K; Stacey S N; Glew S S; Connor M E; Arrand J R; Stern Cancer Research Campaign Department of Immunology, Paterson Institute for Cancer Research, Christie Hospital NHS Trust, Manchester, UK. International journal of cancer. Journal international du cancer, (1993 Feb 20) 53 (4) 591-6. Journal code: 0042124. ISSN: 0020-7136. United States Journal; Article; (JOURNAL ARTICLE) English Priority Journals 199303 Entered STN: 19930402 Last Updated on STN: 19930402 Entered Medline: 19930323 Sera from patients with cervical cancer, cervical intraepithelial neoplasia (CIN) and non-genital cancers, and from healthy individuals, were investigated for antibodies to human papilloma virus (HPV) early proteins E4, E6 and E7 and the major capsid protein LI by Western blot analysis of recombinant HPV proteins. There was a significantly higher prevalence of sera with antibodies to E6 in cervical cancer patients than in healthy individuals or in CIN or non-genital-cancer patients. Antibodies to E7 were

detected in 25% of cervical-cancer patients, which is significantly higher

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than in HPV-associated cervical lesions or in control populations, but not significantly different from the incidence in patients with non-genital cancers. Antibodies to LI were found more frequently in CIN, while antibodies to E4 had a similar prevalence in cervical-cancer, cervical-dysplasia and non-genital-cancer groups, with 24% in the controls. The inability to detect antibodies to E6 and E7 in the majority of cervical-cancer patients limits the application of this methodology to the monitoring of HPV infection and the development of cervical cancer. However, the latter approach may be useful in combination with other assay systems which allow detection of different, including conformational, epitopes of HPV E6 and/or E7 recombinant proteins. Check Tags: Female; Human; Support, Non-U.S. Gov't Adult Aged \*Antibodies, Viral: IM, immunology Blotting, Western Cervix Diseases: IM, immunology Cervix Diseases: MI, microbiology \*Cervix Neoplasms: IM, immunology Cervix Neoplasms: MI, microbiology

Middle Aged

CT

Oncogene Proteins, Fusion: IM, immunology \*Oncogene Proteins, Viral: IM, immunology

\*Papillomavirus: IM, immunology

\*Tumor Virus Infections: IM, immunology

- CN 0 (Antibodies, Viral); 0 (E6 protein, Human papillomavirus type 16); 0 (Oncogene Proteins, Fusion); 0 (Oncogene Proteins, Viral); 0 (oncogene protein E1--E4, Human papillomavirus type 16); 0 (oncogene protein E7, human papillomavirus type 16)
- L9 ANSWER 9 OF 11 MEDLINE on STN
- AN 93019057 MEDLINE
- DN PubMed ID: 1328490
- TI Expression of human papillomavirus type 16 **E6** protein by recombinant baculovirus and use for detection of anti-**E6** antibodies in human sera.
- AU Stacey S N; Bartholomew J S; Ghosh A; Stern P L; Mackett M; Arrand J R
- CS Cancer Research Campaign Department of Molecular Biology, Paterson Institute for Cancer Research, Christie Hospital, Manchester, U.K.
- SO Journal of general virology, (1992 Sep) 73 ( Pt 9) 2337-45. Journal code: 0077340. ISSN: 0022-1317.
- CY ENGLAND: United Kingdom
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 199211
- ED Entered STN: 19930122 Last Updated on STN: 19930122 Entered Medline: 19921104
- AB Existing assays to detect antibodies to human papillomavirus type 16 (HPV-16) proteins in sera from cervical carcinoma patients rely primarily on bacterially produced recombinant proteins or synthetic peptides for use as target antigens. These methods have had limited success in the detection of antibodies against the E6 protein. To produce more authentic E6 protein for use in serological assays, we have employed a recombinant baculovirus vector to synthesize the protein in insect cells. Cells infected with the vector containing E6 gene sequences expressed a stable protein doublet comprising 18.5K and 19.1K bands. This protein reacted in Western blots with an antiserum raised against a purified E6 fusion protein produced in Escherichia

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coli. This antiserum, and several others raised against E. coli-derived
E6 fusion proteins, were unable to recognize the baculovirus
E6 protein in radioimmunoprecipitation assays (RIPAs). However,
serum from a cervical carcinoma patient readily immunoprecipitated the
baculovirus E6 protein, suggesting that the baculovirus-derived
protein represented a realistic antigenic target. A RIPA was developed
for the detection of anti-E6 protein antibodies in
human sera. The assay was tested on a selected group of sera from
carcinoma patients and controls, in comparison with a Western blotting
method using bacterial fusion proteins. The baculovirus E6
protein-based RIPA showed a marked increase in detection rate over the
Western blotting method. These findings suggest that serum
antibodies to HPV-16 E6 protein may
be more prevalent than has previously been shown.
Check Tags: Female; Human; Support, Non-U.S. Gov't
  *Antibodies, Viral: AN, analysis
 Antigens, Viral: IM, immunology
 Baculoviridae: GE, genetics
 Base Sequence
 Carcinoma: MI, microbiology
 Cervix Neoplasms: MI, microbiology
 Molecular Sequence Data
*Oncogene Proteins, Viral: BI, biosynthesis
 Oncogene Proteins, Viral: GE, genetics
*Papillomavirus: GE, genetics
 Precipitin Tests
 Radioimmunoassay
 Recombinant Proteins: BI, biosynthesis
 Recombinant Proteins: IM, immunology
*Tumor Virus Infections: DI, diagnosis
 Tumor Virus Infections: GE, genetics
 Tumor Virus Infections: IM, immunology
0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (E6
protein, Human papillomavirus type 16); 0 (Oncogene Proteins, Viral); 0
(Recombinant Proteins)
ANSWER 10 OF 11
                    MEDLINE on STN
92105325
            MEDLINE
PubMed ID: 1722219
Human papillomavirus type 18 E6 and E7 antibodies in
human sera: increased anti-E7 prevalence in cervical cancer patients.
Bleul C; Muller M; Frank R; Gausepohl H; Koldovsky U; Mgaya H N; Luande J;
Pawlita M; ter Meulen J; Viscidi R; +
Deutsches Krebsforschungszentrum, Heidelberg, Germany.
Journal of clinical microbiology, (1991 Aug) 29 (8) 1579-88.
Journal code: 7505564. ISSN: 0095-1137.
United States
Journal; Article; (JOURNAL ARTICLE)
English
Priority Journals
199202
Entered STN: 19920302
Last Updated on STN: 19960129
Entered Medline: 19920211
Antibody-reactive regions on the human papillomavirus type 18
(HPV-18) E6 and E7 proteins were identified with rabbit
polyclonal anti-fusion protein sera by screening of an fd phage expression
library containing subgenomic HPV-18 DNA fragments and by testing of
overlapping decapeptides representing the E6 and E7 open reading
frames. Peptides comprising the delineated regions (designated E6
/1 to E6/4 and E7/1) were synthesized and used in an
enzyme-linked immunosorbent assay (ELISA) to detect anti-HPV-18
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antibodies in human sera. A total of 232 human serum samples
(identical numbers of cervical cancer patients and age-matched controls)
collected in Tanzania were tested. Similar prevalences (between 0.8 and
4.3%) of antibodies recognizing the different E6
peptides were found in the sera from tumor patients and controls. With a
synthetic 28-mer peptide (designated pepE701) comprising the E7/1 region,
a significant difference was found: 10 of 116 tumor serum samples but 0 of
116 control serum samples showed a specific reaction (P less than 0.001).
This observation confirms earlier results with HPV-16
E7 fusion proteins (I. Jochmus-Kudielka, A. Schneider, R. Braun, R.
Kimmig, U. Koldovsky, K. E. Schneweis, K. Seedorf, and L. Gissmann, J. Natl. Cancer Inst. 81:1698-1704, 1989). A lower prevalence of
anti-HPV-18 E7 antibodies was observed when 188 human serum
samples collected in Germany from tumor patients and controls were tested
(3 of 94 positive in the cancer group; 0 of 94 positive in the control
group). The type specificity of anti-HPV-18 E7 antibodies was
demonstrated when the HPV type found by Southern hybridization in the
cervical cancer biopsies was compared with seroreactivity: 4 of 8 serum
samples obtained from HPV-18 DNA-positive but 0 of 16 serum samples from
HPV-18 DNA-negative tumor patients reacted in the HPV-18 E7 ELISA. In
addition, HPV-18-positive sera failed to react in a peptide ELISA with the
homologous HPV-16 E7 region (M. Muller, H.
Gausepohl, G. de Martinoff, R. Frank, R. Brasseur, and L. Gissmann, J.
Gen. Virol. 71:2709-2717, 1990) and vice versa.
Check Tags: Female; Human; Support, Non-U.S. Gov't
 Amino Acid Sequence
   Antibody Specificity
 Bacteriophages: GE, genetics
 Base Sequence
 Cervix Neoplasms: DI, diagnosis
*Cervix Neoplasms: IM, immunology
 Chromosome Mapping
 Cloning, Molecular
 DNA Probes
 Enzyme-Linked Immunosorbent Assay
 Epitopes: GE, genetics
 Gene Library
 Molecular Sequence Data
 Oncogene Proteins, Viral: GE, genetics
*Oncogene Proteins, Viral: IM, immunology
 Open Reading Frames: GE, genetics
*Papillomavirus: IM, immunology
0 (DNA Probes); 0 (E6 protein, Human papillomavirus type 18); 0
(E7 protein, Human papillomavirus type 18); 0 (Epitopes); 0 (Oncogene
Proteins, Viral)
ANSWER 11 OF 11
                    MEDLINE on STN
91220701
           MEDLINE
PubMed ID: 1850917
Expression of human papillomavirus proteins in yeast Saccharomyces
Carter J J; Yaegashi N; Jenison S A; Galloway D A
Fred Hutchinson Cancer Research Center, Seattle, Washington 98104.
CA 35568 (NCI)
CA 42792 (NCI)
CA01391 (NCI)
Virology, (1991 Jun) 182 (2) 513-21.
Journal code: 0110674. ISSN: 0042-6822.
United States
Journal; Article; (JOURNAL ARTICLE)
English
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Priority Journals

EM 199106

ED Entered STN: 19910623

Last Updated on STN: 19910623

Entered Medline: 19910606

AΒ The L1 and L2 proteins of human papillomavirus (HPV) types 1, 6, and 16 and the E6 and E7 proteins of HPV 16 were expressed in Saccharomyces cerevisiae. The yeast expressed proteins were readily detected by immune blotting and were generally intact. The HPV 1 L1 and L2 proteins expressed in yeast were indistinguishable from the major and minor capsid proteins purified from HPV 1 virions as judged by gel electrophoresis and immunoblotting. The HPV 6 and HPV 16 L2 proteins and HPV 16 E7 proteins were secreted from yeast by fusion to the yeast pre-pro-alpha-factor leader sequence. Following secretion of the HPV 16 E7 protein a rapid method of purification was developed. The yeast expressed proteins were used as antigen targets to study the human immune response in Western blot assay, ELISA, and immune precipitation. One human serum reacted with intact, but not denatured HPV 16 L2 proteins, suggesting that the yeast expressed proteins will be useful to detect antibodies reactive with conformational epitopes.

Check Tags: Human; In Vitro; Support, U.S. Gov't, P.H.S.

Antibodies, Viral: IM, immunology
\*Antigens, Viral: GE, genetics
Cloning, Molecular
Gene Expression
Glycoproteins: GE, genetics

- T.11 ANSWER 1 OF 9 MEDLINE on STN
- 2002057513 ANMEDLINE
- DN PubMed ID: 11783091
- Detection of HPV in human esophageal cancer in high-incidence area and its ΤI correlation with p53 expression.
- Lu Z; Chen K; Guo M ΑU
- Department of Genetics, Beijing Institute for Cancer Research, Tumor CS Hospital, Beijing University, Beijing 100034, China.
- SO Zhonghua zhong liu za zhi [Chinese journal of oncology], (2001 May) 23 (3) 220-3.

Journal code: 7910681. ISSN: 0253-3766.

- CY China
- DTJournal; Article; (JOURNAL ARTICLE)
- LΑ Chinese
- FS Priority Journals
- EΜ 200203
- Entered STN: 20020125 ED
  - Last Updated on STN: 20020324 Entered Medline: 20020322
- OBJECTIVE: To investigate the association of HPV with the development of AΒ esophageal cancer (EC) in a high-incidence area of EC and to elucidate its correlation with p53 overexpression. METHODS: Thirty EC specimens were collected from Anyang, Henan. Four pairs of primers were designed to perform in situ hybridization (ISH) and in situ PCR(ISPCR). Immunohistochemical staining was used to detect p53. RESULTS: HPV L1, HPV-16-E6 and HPV-16-E7 was detected in 10.0%, 60.0% and 63.3% of the EC samples, respectively. The detection rate of HPV -18-E6 was low(6.7%) and no EBV was detected. Overexpression of p53 was identified in 73.3% EC. With ISH or ISPCR, HPV-16-E6 was positive in 53.3% of EC. CONCLUSION: The low detection rate of HPV L1 and high detection rate of HPV-16-E6 and E7 genes suggest that HPV may be partially lost when integrating into tumor cell genome, while E6 and E7 genes are intact. The results support a role of HPV-16 in the pathogenesis of EC in high incidence area. Although p53 mutation takes an important part in tumor pathogenesis, it is not consistent with the HPV existence in the EC cells.
- CT Check Tags: Human

English Abstract

Esophageal Neoplasms: GE, genetics Esophageal Neoplasms: ME, metabolism

\*Esophageal Neoplasms: VI, virology

In Situ Hybridization

\*Oncogene Proteins, Viral: AN, analysis Oncogene Proteins, Viral: GE, genetics Papillomavirus, Human: CH, chemistry Polymerase Chain Reaction: MT, methods

\*Protein p53: BI, biosynthesis

Protein p53: GE, genetics

- CN 0 (E6 protein, Human papillomavirus type 16); 0 (Oncogene Proteins, Viral); 0 (Protein p53); 0 (oncogene protein E7, human papillomavirus type 16)
- L11 ANSWER 2 OF 9 MEDLINE on STN
- 1998312394 MEDLINE AN
- DN PubMed ID: 9648588
- The status of human papillomavirus and tumor suppressor genes p53 and p16 TΙ in carcinomas of uterine cervix from India.
- ΑU Munirajan A K; Kannan K; Bhuvarahamurthy V; Ishida I; Fujinaga K; Tsuchida N; Shanmugam G
- CS Cancer Biology Division, School of Biological Sciences, Madurai Kamaraj

University, India. Gynecologic oncology, (1998 Jun) 69 (3) 205-9. SO Journal code: 0365304. ISSN: 0090-8258. CY United States DT Journal; Article; (JOURNAL ARTICLE) LA English FS Priority Journals ĒΜ 199807 , Entered STN: 19980723 ED Last Updated on STN: 19980723 Entered Medline: 19980715 AΒ OBJECTIVES: Infection with the high-risk strain of human papillomaviruses (HPVs) and the inactivation of the tumor suppressor gene p53 through mutation are important factors in cervical carcinogenesis. To know whether such events would occur in cervical carcinomas of Indians, 43 tumors (consisting of 36 of stage III B and 6 of stage II B) were screened for p53 and p16 gene mutations. METHODS: PCR followed by single-strand conformation polymorphism (SSCP) analysis were used to detect mutations in p53 and p16 genes and PCR for the presence of human papillomavirus genome. HPV status was ascertained by PCR amplification of parts of E6 and E7 genes using primers pU-1M and pU-2R and typing was carried out by restriction analysis. RESULTS: Of the 43 samples analyzed, 4 samples (9%) showed mobility shifts for p53 mutations; PCR products of the p16 gene did not show band shifts in SSCP analysis. HPV DNA was detected in 70% of the 43 samples analyzed: HPV 16 in 23 cases (53%), HPV 18 in 4 cases (13.3%), and HPV 33 in 1 case (3.3%). Two amplified HPV DNAs that were difficult to type with various . restriction enzymes were cloned and the amplified regions were sequenced. One of these was 93% close to HPV 35 and the other was 80% close to HPV 58. Three samples had both p53 mutations and HPV genome. CONCLUSIONS: Our results indicate that HPV 16 infection was more common than HPV 18, the p53 mutations and HPV infection were not mutually exclusive events in the genesis of carcinoma of uterine cervix among Indian women, and p16 gene may not play a role in Indian cervical carcinomas. CTCheck Tags: Female; Human; Support, Non-U.S. Gov't Adult Aged Cervix Neoplasms: EP, epidemiology Cervix Neoplasms: GE, genetics \*Cervix Neoplasms: VI, virology \*DNA, Viral: AN, analysis \*Genes, p16: GE, genetics \*Genes, p53: GE, genetics Incidence India: EP, epidemiology Middle Aged \*Papillomavirus, Human: GE, genetics \*Papovaviridae Infections: EP, epidemiology Polymerase Chain Reaction Polymorphism; Single-Stranded Conformational \*Tumor Virus Infections: EP, epidemiology CN 0 (DNA, Viral) L11ANSWER 3 OF 9 MEDLINE on STN 1998050245 AN MEDLINE DN PubMed ID: 9388862 ΤI Human papillomavirus infection and esophageal squamous cell carcinoma. ΑU He D; Tsao S W; Bu H CS Department of Anatomy, Faculty of Medicine, University of Hong Kong. SO Zhonghua bing li xue za zhi Chinese journal of pathology, (1996 Dec) 25 (6) 351-4.

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Journal code: 0005331. ISSN: 0529-5807.
CY
     China
DT
     Journal; Article; (JOURNAL ARTICLE)
LΑ
     Chinese
FS
     Priority Journals
EΜ
     199801
ED
     Entered STN: 19980129
     Last Updated on STN: 19980129
     Entered Medline: 19980109
     Human papillomavirus (HPV) infection, especially high risk types HPV 16
AΒ
     and 18, have been studied widely in cervical cancer. However, HPV
     infection in esophageal cancer has not been well defined. In the present
     study, immunohistochemistry, PCR and Southern blot hybridization methods
     were used to detect HPV infection in 127 cases of esophageal
     squamous cell carcinoma. Immunohistochemistry results indicated that the
     virus was detected frequently in well differentiated carcinoma.
     positive rates for BPV and HPV E6 protein were 60.6% (77/127)
     and 43% (54/127) respectively. Meanwhile, PCR and Southern hybridization
     showed that 35.9% (37/103) of esophageal squamous cell carcinomas have HPV
     DNA, which included 20.4% (21/103) HPV 16 and 7.8% (8/103) HPV
          Of the 103 cases, only 1 had both HPV 16 and HPV
     18 DNA. Our results suggest that HPV infection is present in
     esophageal squamous cell carcinoma and may play a role in its
     pathogenesis.
     Check Tags: Human; Male
CT
      Adult
      Aged
      Aged, 80 and over
      Antibodies, Viral: AN, analysis
     *Carcinoma, Squamous Cell: VI, virology
      DNA, Viral: AN, analysis
      English Abstract
     *Esophageal Neoplasms: VI, virology
      Middle Aged
      Oncogene Proteins, Viral: BI, biosynthesis
     *Papillomavirus, Human: IP, isolation & purification
     *Papovaviridae Infections
     *Tumor Virus Infections
CN
     0 (Antibodies, Viral); 0 (DNA, Viral); 0 (E6 protein, Human
     papillomavirus type 16); 0 (Oncogene Proteins, Viral)
L11 ANSWER 4 OF 9
                       MEDLINE on STN
AN
     95146374
                  MEDLINE
     PubMed ID: 7843998
DN
     [Inverted papilloma and its association with human papillomavirus (HPV). A
ΤI
     study with polymerase chain reaction (PCR)].
     Das inverte Papillom und seine Assoziation mit dem humanen Papillomvirus
     (HPV). Eine Studie mit der "polymerase chain reaction" (PCR).
CM
     Comment in: HNO. 1994 Nov; 42(11):663-4. PubMed ID: 7843996
ΑU
     Arndt O; Nottelmann K; Brock J; Neumann O G
CS
     HNO-Abteilung des Marienkrankenhauses, Hamburg.
SO
     HNO, (1994 Nov) 42 (11) 670-6.
     Journal code: 2985099R. ISSN: 0017-6192.
CY
     GERMANY: Germany, Federal Republic of
DT
     Journal; Article; (JOURNAL ARTICLE)
LA
     German
FS
     Priority Journals
EΜ
     199503
ED
     Entered STN: 19950316
     Last Updated on STN: 19950316
     Entered Medline: 19950308
AΒ
     Nasal inverted papilloma is usually a benign tumor but is associated with
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squamous cell carcinoma in about 10% of cases. To determine the etiological role of human papillomavirus (HPV) in inverted papilloma and to clarify the relationship between the different types of human papillomavirus and malignant transformation, we analyzed retrospectively a series of 29 formalin - fixed, paraffin-embedded cases, 3 of which had squamous cell carcinoma. A highly sensitive and specific modification of the polymerase chain reaction (PCR) was used to detect the E6 gene sequences of HPV 6/11, 16 and 18. HPV was present in 20 of the cases (69%), HPV 6/11 in 14 (48%), HPV 16 in 19 (65%) and both HPV 6/11 and 16 in 13 of the specimens (45%). HPV 18 was not identified in any specimen. In all three of the squamous cell carcinomas based on inverted papillomas, HPV 6/11 and 16 were detected. These results were in agreement with other studies. While HPV is related etiologically to inverted papilloma, we suggest that HPV 16 may be involved in its malignant transformation. Check Tags: Female; Human; Male; Support, Non-U.S. Gov't Adult Aged Aged, 80 and over Carcinoma, Squamous Cell: GE, genetics \*Carcinoma, Squamous Cell: PA, pathology Cell Transformation, Neoplastic: GE, genetics Cell Transformation, Neoplastic: PA, pathology Cell Transformation, Viral: GE, genetics English Abstract Middle Aged Nose Neoplasms: GE, genetics \*Nose Neoplasms: PA, pathology Papilloma, Inverted: GE, genetics \*Papilloma, Inverted: PA, pathology Papillomavirus, Human: CL, classification \*Papillomavirus, Human: GE, genetics Papovaviridae Infections: GE, genetics \*Papovaviridae Infections: PA, pathology \*Polymerase Chain Reaction: MT, methods Retrospective Studies Tumor Virus Infections: GE, genetics \*Tumor Virus Infections: PA, pathology ANSWER 5 OF 9 MEDLINE on STN 94064167 MEDLINE PubMed ID: 8244575 Serologic response in human papillomavirus-associated invasive cervical cancer. Viscidi R P; Sun Y; Tsuzaki B; Bosch F X; Munoz N; Shah K V Eudowood Division of Infectious Disease, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD. R01-CA56514 (NCI) International journal of cancer. Journal international du cancer, (1993 Nov 11) 55 (5) 780-4. Journal code: 0042124. ISSN: 0020-7136. United States Journal; Article; (JOURNAL ARTICLE) English Priority Journals 199312 Entered STN: 19940201 Last Updated on STN: 19940201

CT

L11

AN

DN

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ΕM

ED

Entered Medline: 19931223

AB Human papillomavirus (HPV) transforming proteins **E6** and E7 are uniformly expressed in HPV-associated cervical cancer. Our objective was to measure antibodies to HPV-16 **E6** and E7 proteins in cervical

cancer patients using an assay which would detect antibodies to conformational epitopes. Serum specimens obtained from two case-control studies of HPVs and cervical cancer were tested. The studies were performed in Cali, Colombia, South America and in 9 provinces of Spain. Cases consisted of women with invasive cervical cancer associated with HPV-16 or other HPV types and women with HPV-16-associated high-grade cervical intra-epithelial neoplasia (CIN-3). Controls for invasive cases and CIN-3 cases were women who had no cytologic abnormalities and who were matched for age and country of residence. Serum antibodies to HPV-16 E6 and E7 proteins were detected by radio-immunoprecipitation of in vitro translated proteins. Antibodies to the E6 and E7 protein were observed among 56% and 43%, respectively, of invasive cases and 1.7% and 4.1%, respectively, of controls. Antibodies to either protein were detected in 72% of sera from invasive cases and 5.8% of sera from controls. High antibody reactivity and antibodies to both proteins were found almost exclusively in invasive cases. The frequency of antibodies to the  ${\tt E6}$  protein and the E7 protein among CIN-3 cases did not differ significantly from the CIN-3 controls. Five women with HPV-18-associated invasive cervical cancer were negative for serum antibody to HPV-16 E6 and E7 proteins. Antibodies to HPV-16 E6 and E7 proteins appear to be partially virus-specific and disease state-specific markers of HPV-associated cervical cancer.

- CT Check Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
  - \*Antibodies, Viral: BL, blood

Case-Control Studies

- \*Cervical Intraepithelial Neoplasia: IM, immunology
- \*Cervical Intraepithelial Neoplasia: MI, microbiology
- \*Cervix Neoplasms: IM, immunology
- \*Cervix Neoplasms: MI, microbiology

Colombia

Immunosorbent Techniques

Oncogene Proteins, Viral: IM, immunology

\*Papillomavirus, Human

Spain

- CN 0 (Antibodies, Viral); 0 (E6 protein, Human papillomavirus type 16); 0 (Oncogene Proteins, Viral); 0 (oncogene protein E7, human papillomavirus type 16)
- L11 ANSWER 6 OF 9 MEDLINE on STN
- AN 93175190 MEDLINE
- DN PubMed ID: 1337817
- TI Detection of human papillomavirus DNA in invasive cervical cancers by the polymerase chain reaction and its clinical significance.
- AU Kashiwabara K; Nakajima T
- CS Second Department of Pathology, Gunma University School of Medicine, Japan.
- SO Acta pathologica japonica, (1992 Dec) 42 (12) 876-83. Journal code: 0372637. ISSN: 0001-6632.
- CY Japan
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 199303
- ED Entered STN: 19930402

Last Updated on STN: 19930402

Entered Medline: 19930323

AB In order to **detect** human papillomavirus (HPV) DNA in invasive cervical cancers, three different polymerase chain reactions to amplify different subgenomic fragments of HPV DNA were carried out on DNA extracted from 93 formalin-fixed and paraffin-embedded tumor tissues.

This study detected HPV DNA in 54 cases (58.1%), which broke down to HPV 16 in 39 (41.9%) cases, HPV 18 in six (6.4%), HPV 52 in three, HPV 33 in one and unclassified HPV type in the remainder. Histopathologically, squamous cell carcinomas frequently contained HPV 16, whereas, HPV 18 was present in adenocarcinoma, adenosquamous cell carcinoma and small cell carcinoma of the cervix. Clinicopathological study revealed that HPV 16 and 18 DNA found were more frequently than other HPV subtypes in premenopausal patients. Moreover, HPV 18 DNA-positive cancers had a relatively high recurrence rate. These results indicate that cervical cancers might be clinically influenced by the difference in subtypes of the infecting HPV. Check Tags: Female; Human; Support, Non-U.S. Gov't \*Adenocarcinoma: GE, genetics Amino Acid Sequence \*Carcinoma, Squamous Cell: GE, genetics \*Cervix Neoplasms: GE, genetics \*DNA, Viral: AN, analysis Menopause Molecular Sequence Data Oncogene Proteins, Viral: GE, genetics \*Papillomavirus: GE, genetics \*Polymerase Chain Reaction 0 (DNA, Viral); 0 (E6 protein, Human papillomavirus type 16); 0 (E7 protein, Human papillomavirus type 18); 0 (Oncogene Proteins, Viral); 0 (oncogene protein E7, human papillomavirus type 16) L11 ANSWER 7 OF 9 MEDLINE on STN 92397155 MEDLINE PubMed ID: 1326129 Polymerase chain reaction for producing biotinylated human papillomavirus DNA probes for in situ hybridization. Syrjanen S; Andersson B; Juntunen L; Syrjanen K Department of Pathology, University of Kuopio, Finland. Sexually transmitted diseases, (1992 May-Jun) 19 (3) 140-5. Journal code: 7705941. ISSN: 0148-5717. United States Journal; Article; (JOURNAL ARTICLE) English Priority Journals 199210 Entered STN: 19921023 Last Updated on STN: 19921023 Entered Medline: 19921013 Polymerase chain reaction (PCR) was used to produce biotinylated DNA probes for human papillomavirus (HPV) types 16 and 18. The specificity and sensitivity of the probes were tested with in situ hybridization to detect HPV DNA in cervical biopsies or cell lines (CaSki, SiHa, and HeLa). The Gene Amp DNA Amplification kit (Perkin-Elmer Cetus, Norwalk, CT) was used to perform PCR according to the manufacturer's instructions, except that dTTP was substituted by different concentrations of biotinylated dUTP (bio-11-UTP). As the template DNA, the DNA extracted either from CaSki or HeLa cells was used. The reaction mixture was taken through up to 40 cycles of amplification in a Perkin-Elmer Cetus Thermal Cycler (Perkin-Elmer Cetus, Norwalk, CT). The highest yield was achieved when the concentrations of dTTP and biotinylated dUTP were 150 microM and 50 microM, respectively. In situ hybridization results compatible with those obtained with biotinylated or radioactively labelled whole genomic HPV DNA probes were demonstrated when primers from E6, E7, and L1 ORF of the HPV 18 were used to produce the biotinylated probe by PCR. With HPV 16, the positive signals were always weaker with the PCR probe than with the whole genomic probe. Overall, the

PCR probes might have a lower sensitivity than the whole genomic probes.

CT

CN

AN

DN

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CS

SO

CY

DTLΑ

FS EΜ

ED

AΒ

The background stain was always stronger with the PCR probes than with the whole genomic probes, especially with HPV 16 probes. There does not seem to be a clear correlation between the sensitivity of PCR probes and the size or nucleotide content of the probe. Check Tags: Comparative Study; Female; Human; Support, Non-U.S. Gov't Base Sequence Biotin Cell Line Cervix Neoplasms: DI, diagnosis \*DNA Probes: CS, chemical synthesis DNA Probes: GE, genetics Molecular Sequence Data Nucleic Acid Hybridization \*Papillomavirus: GE, genetics \*Polymerase Chain Reaction: MT, methods Sensitivity and Specificity \*Tumor Virus Infections: DI, diagnosis 58-85-5 (Biotin) 0 (DNA Probes) L11 ANSWER 8 OF 9 MEDLINE on STN 92148562 MEDLINE PubMed ID: 1664460 HPV in full thickness cervical biopsies: high prevalence in CIN 2 and CIN 3 detected by a sensitive PCR method. Arends M J; Donaldson Y K; Duvall E; Wyllie A H; Bird C C Department of Pathology, University Medical School, Edinburgh, U.K. Journal of pathology, (1991 Dec) 165 (4) 301-9. Journal code: 0204634. ISSN: 0022-3417. ENGLAND: United Kingdom Journal; Article; (JOURNAL ARTICLE) English Priority Journals 199203 Entered STN: 19920405 Last Updated on STN: 19920405 Entered Medline: 19920317 A new type-specific, sensitive, non-radioactive assay is described for the detection of human papillomavirus (HPV) DNA in tissues. Sequences within the **E6** gene were amplified by the polymerase chain reaction (PCR), using primer pairs which clearly distinguish HPV types, including those with close sequence homology such as 6b and 11. The amplified DNA products were identified by non-radioactive oligonucleotide hybridization and restriction endonuclease mapping, and the method was sufficiently sensitive to detect between 3 and 5 SiHa cells (each containing 1-2 copies of HPV 16 DNA) amongst 10,000 non-HPV-containing cells. Frozen

AB and archival paraffin sections were equally acceptable substrates for the reaction. The assay was applied to frozen sections of full thickness cervical epithelium from 60 cases of cervical intraepithelial neoplasia (CIN) and 24 normal cervical controls. HPV DNA was detected in 60 per cent of cases of CIN 3 and CIN 2, in 25 per cent of cases of CIN 1, and in none of the normal controls. Prevalence of HPV 16 was similar (approximately 50 per cent) in both CIN 2 and CIN 3, and in the whole series HPV 16 was almost five-fold more common than HPV 18. Low-risk HPV types were present in 5 per cent of CIN 1, but 0 per cent of CIN 2 and CIN 3 biopsies. The data emphasize the biological similarity of CIN 2 and CIN 3 lesions, and their divergence from CIN 1. CTCheck Tags: Female; Human; Support, Non-U.S. Gov't

Adolescent

CT

RN

CN

AN

DN

TI

ΑU

CS

SO

CY

DT

LA

FS

EM

ED

Adult

Base Sequence

\*Cervix Neoplasms: MI, microbiology

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Cervix Neoplasms: PA, pathology
     *Cervix Uteri: MI, microbiology
      Cervix Uteri: PA, pathology
      DNA, Viral: AN, analysis
      Middle Aged
      Molecular Sequence Data
      Papillomavirus: CL, classification
      Papillomavirus: GE, genetics
     *Papillomavirus: IP, isolation & purification
     *Polymerase Chain Reaction: MT, methods
CN
     0 (DNA, Viral)
L11 ANSWER 9 OF 9
                       MEDLINE on STN
AN
     92105325
                 MEDLINE
     PubMed ID: 1722219
DN
ΤI
     Human papillomavirus type 18 E6 and E7 antibodies in human sera:
     increased anti-E7 prevalence in cervical cancer patients.
     Bleul C; Muller M; Frank R; Gausepohl H; Koldovsky U; Mgaya H N; Luande J;
ΑU
     Pawlita M; ter Meulen J; Viscidi R; +
     Deutsches Krebsforschungszentrum, Heidelberg, Germany.
CS
     Journal of clinical microbiology, (1991 Aug) 29 (8) 1579-88.
SO
     Journal code: 7505564. ISSN: 0095-1137.
CY
     United States
     Journal; Article; (JOURNAL ARTICLE)
DT
LΑ
     English
FS
     Priority Journals
EM
     199202
ED
     Entered STN: 19920302
     Last Updated on STN: 19960129
     Entered Medline: 19920211
AΒ
     Antibody-reactive regions on the human papillomavirus type 18 (HPV
     -18) E6 and E7 proteins were identified with rabbit
     polyclonal anti-fusion protein sera by screening of an fd phage expression
     library containing subgenomic HPV-18 DNA fragments and
     by testing of overlapping decapeptides representing the E6 and
     E7 open reading frames. Peptides comprising the delineated regions
     (designated E6/1 to E6/4 and E7/1) were synthesized
     and used in an enzyme-linked immunosorbent assay (ELISA) to detect
     anti-HPV-18 antibodies in human sera. A total of 232
     human serum samples (identical numbers of cervical cancer patients and
     age-matched controls) collected in Tanzania were tested. Similar
     prevalences (between 0.8 and 4.3%) of antibodies recognizing the different
     E6 peptides were found in the sera from tumor patients and
     controls. With a synthetic 28-mer peptide (designated pepE701) comprising
     the E7/1 region, a significant difference was found: 10 of 116 tumor serum
     samples but 0 of 116 control serum samples showed a specific reaction (P
     less than 0.001). This observation confirms earlier results with HPV-16
     E7 fusion proteins (I. Jochmus-Kudielka, A. Schneider, R. Braun, R. Kimmig, U. Koldovsky, K. E. Schneweis, K. Seedorf, and L. Gissmann,
     J. Natl. Cancer Inst. 81:1698-1704, 1989). A lower prevalence of anti-
     HPV-18 E7 antibodies was observed when 188 human serum
     samples collected in Germany from tumor patients and controls were tested
     (3 of 94 positive in the cancer group; 0 of 94 positive in the control
             The type specificity of anti-HPV-18 E7
     antibodies was demonstrated when the HPV type found by Southern
     hybridization in the cervical cancer biopsies was compared with
     seroreactivity: 4 of 8 serum samples obtained from HPV-
     18 DNA-positive but 0 of 16 serum samples from HPV-
     18 DNA-negative tumor patients reacted in the HPV-
     18 E7 ELISA. In addition, HPV-18-positive
     sera failed to react in a peptide ELISA with the homologous HPV-16 E7
     region (M. Muller, H. Gausepohl, G. de Martinoff, R. Frank, R.
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Brasseur, and L. Gissmann, J. Gen. Virol. 71:2709-2717, 1990) and vice versa.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't

Amino Acid Sequence Antibody Specificity

Bacteriophages: GE, genetics

### => d his

## (FILE 'HOME' ENTERED AT 14:57:46 ON 29 NOV 2004)

# FILE 'MEDLINE' ENTERED AT 14:57:53 ON 29 NOV 2004

		E	HU Y X/AU
L1	21	S	E3
L2	1	S	VIRUS AND L1
L3	150	S	HPV-16 AND E
L4	. 10	S	DETECT AND L3
L5	150	S	HPV-16 AND "E"
L6	786	S	HPV-16 AND "E6"
L7	108337	S	DETECT OR DETECTING AND L6
L8	41	S	DETECT AND L6
L9	11	S	ANTIBOD? AND L8
L10	239	S	HPV-18 AND "E6"
L11	9	S	DETECT AND L10

```
L9
     ANSWER 1 OF 11
                        MEDLINE on STN
     2001557983
                    MEDLINE
AN
DN
     PubMed ID: 11604112
     Generation and characterization of monoclonal antibodies against
ΤI
     the E6 and E7 oncoproteins of HPV.
     Wlazlo A P; Giles-Davis W; Clements A; Struble G; Marmorstein R; Ertl H C
ΑU
     The Wistar Institute, Philadelphia, PA 19104, USA.
CS
     Hybridoma, (2001 Aug) 20 (4) 257-63.
SO
     Journal code: 8202424. ISSN: 0272-457X.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
LΑ
     English
     Priority Journals
FS
     200201
EM
     Entered STN: 20011018
ED
     Last Updated on STN: 20020125
     Entered Medline: 20020117
AB
     Generation of three monoclonal antibodies (MAbs) to the major
     oncoproteins of human papillomavirus (HPV) was accomplished by an intense
     prime/boost regimen. Mice were primed with expression vectors expressing
     either the E6 or E7 oncoproteins of HPV-16
     followed by boosting with a vaccinia virus construct and a
     replication-defective El-deleted adenoviral recombinant of the human
     strain 5, and last, with baculovirus-derived HPV-16
    E6 and E7 proteins in incomplete Freunds' adjuvant. Splenocytes were then fused with a myeloma cell line. The vaccination protocol
     generated one anti-E7 MAb of the IgM isotype and two anti-E6
     MAbs of the IgG1 subisotype. The MAbs were tested for functionality in
     standard laboratory assays and found to detect the E6
     and E7 proteins, respectively. The E7 MAb cross-reacted with the HPV-la
     E7 oncoprotein. The binding sites of the MAbs were mapped to defined
     regions of each viral protein.
CT
     Check Tags: Female; Human; Support, Non-UaS. Gov't; Support, U.S. Gov't,
     P.H.S.
      Amino Acid Sequence
      Animals
        Antibodies, Monoclonal: AN, analysis
       *Antibodies, Monoclonal: BI, biosynthesis
        Antibodies, Viral: AN, analysis
       *Antibodies, Viral: BI, biosynthesis
        Antibody Formation
     *Antigens, Viral: IM, immunology Blotting, Western
      Cells, Cultured
      DNA Primers: CH, chemistry
      Enzyme-Linked Immunosorbent Assay
      Epitope Mapping
     Mice
     Mice, Inbred BALB C
     Mice, SCID
     Molecular Sequence Data
     *Oncogene Proteins, Viral: IM, immunology
     Oncogene Proteins, Viral: IP, isolation & purification
     *Papillomavirus: IM, immunology
      Peptide Fragments: IM, immunology
      Polymerase Chain Reaction
      Sequence Homology, Amino Acid
CN
     0 (Antibodies, Monoclonal); 0 (Antibodies, Viral); 0
     (Antigens, Viral); 0 (DNA Primers); 0 (E6 protein, Human
     papillomavirus type 16); 0 (Oncogene Proteins, Viral); 0 (Peptide
```

- L2 ANSWER 1 OF 1 MEDLINE on STN
- AN 94306962 MEDLINE
- DN PubMed ID: 8033617
- TI Diagnosis between condyloma acuminatum and pseudocondyloma in lower female genital tract as determined by a PCR-based method.
- AU Fu Y L; Hu Y X; Lin H L
- CS Guangzhou Maternal and Neonatal Hospital.
- SO Zhonghua fu chan ke za zhi, (1994 Jan) 29 (1) 16-8, 59-60. Journal code: 16210370R. ISSN: 0529-567X.
- CY China
- DT (CLINICAL TRIAL)

  Journal; Article; (JOURNAL ARTICLE)

  (RANDOMIZED CONTROLLED TRIAL)
- LA Chinese
- FS Priority Journals
- EM 199408
- ED Entered STN: 19940825

Last Updated on STN: 19940825 Entered Medline: 19940812

#### => d 12 ab

- L2 ANSWER 1 OF 1 MEDLINE on STN
- From Jan. 1990-Aug. 1992, 616 patients with papillomatous growth of the AB lower female genital tract (the nodular type 307 cases, the papular type 309 cases) were investigated as determined by a PCR (polymerase chain reaction) -based method, associated with immunohistochemistry avidin biotin complex (ABC), electron microscopy, histopathology, colposcopy and clinical follow-up. The PCR is the most sensitive and specific method. Using PCR the HPV DNA 6.11.16.18.33 were positive in 97.90% of the nodular type. However HPV DNA were positive in 1.10% of the papular type. In the patients with both type, HPV DNA were also positive in nodular, but negative in papular. In the nodular type the HPV-Ag present in 53.55% by ABC method, the koilocytes were 70.49% by microscopy, HPV particles were seen in 5 out of 85 samples by electron microscopy. So that the nodular type (typical cauliflower like) is genital warts (condyloma acuminatum) by HPV infection. The papular type (typical papular or finger like) growth on the mucosal surface of the labia minora of lower vagina. They were negative for HPV DNA, HPV-Ag, HPV particles and koilocytes. On follow-up observation for 3 months to 2 years they had not developed to nodular type and no sexually transmitted feature was observed. The papular type is pseudocondyloma.

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ANSWER 2 OF 11
                        MEDLINE on STN
L9
AN
     1998240895
                    MEDLINE
DN
     PubMed ID: 9570998
TΙ
     HPV-16-related proteins as the serologic markers in
     cervical neoplasia.
     Park J S; Park D C; Kim C J; Ahn H K; Um S J; Park S N; Kim S J; Namkoong
ΑU
     Department of Obstetrics and Gynecology, Catholic University Medical
CS
     College, Catholic Cancer Center, Seoul, Korea.
     Gynecologic oncology, (1998 Apr) 69 (1) 47-55.
SQ
     Journal code: 0365304. ISSN: 0090-8258.
CY
     United States
     Journal; Article; (JOURNAL ARTICLE)
DT
LA
     English
FS
     Priority Journals
     199805
EM
     Entered STN: 19980529
ED
     Last Updated on STN: 19990129
     Entered Medline: 19980519
AΒ
     OBJECTIVE: Recently, a variety of HPV-related proteins have been
     synthesized and their utility as diagnostic and prognostic markers in
     cervical cancers needs to be assessed. The ability to generate
     preparative amounts of HPV-16 L1/L2 VLPs and
     E6, E7 proteins may have implications for the development of a
     serologic assay to detect anti-HPV-16 virion
     immune responses. The purpose of the study is to improve the way of
     proper management of the cervical cancer by investigating the utility of
     the recently developed HPV-16 L1/L2 VLPs, HPV
     -16 E6, E7 proteins as the clinical serologic markers
     through antibody reactions by comparison with those of SCCA and
     CEA which have been used as tumor markers for cervical cancer. METHODS:
     The serologic responses in Korean women with cervical neoplasia by ELISA
     using HPV-16 L1/L2 VLPs and radioimmunoprecipitation
     assay (RIPA) using in vitro translated HPV-16
    E6, E7 proteins were investigated. PCR using E6
     type-specific primers for HPV-16/18 was used to
     determine the presence and type of HPV infection (normal controls, 15
     cases; preinvasive lesions, 28 cases; invasive cervical cancers, 124
     cases). RESULTS: The sera of 34% (42/124) of cervical cancers were
     positive for SCCA and the sera of 18% (22/124) of cervical cancers were
    positive for CEA. The positivity of SCCA was increased with advancing
     clinical stages, but the antibody levels were not correlated
     with clinical stage of disease. The sera of 7% (1/15) of normal controls,
     39% (11/28) of preinvasive lesions, and 56% (70/124) of patients with
     cervical cancer were ELISA positive for HPV-16 L1/L2
    VLPs (P < 0.05). The sera of 7\% (2/28) of preinvasive lesions and 51\%
     (63/124) of cervical cancers were positive for in vitro translated
     HPV-16 E6 protein (P < 0.05) and the sera of
     11% (3/28) of preinvasive lesions and 33% (41/124) of cervical cancers
     were positive for in vitro translated HPV-16 E7
     protein (P < 0.05). The antibody levels to HPV-
     16 E7 protein were correlated to clinical stage and tumor burden
     in a significant number of cervical cancers. CONCLUSIONS: These data
     suggest that a considerable number of patients with cervical neoplasia
     generated positive antibody response to L1/L2 VLPs and in vitro
     translated E6, E7 proteins of HPV-16. These
    HPV-16-associated proteins might be disease-specific
    markers which could be useful in an adjunctive diagnostic assay and a
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seroepidemiologic study of HPV-related cervical neoplasia. In particular,

the monitoring of antibody to HPV-16 E7

# **Hit List**

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**Search Results -** Record(s) 1 through 3 of 3 returned.

1. Document ID: SU 1731336 A1

L14: Entry 1 of 3

File: DWPI

May 7, 1992

DERWENT-ACC-NO: 1993-132331

DERWENT-WEEK: 199316

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TITLE: Automated line for horizontal metal tubes, etc. pressing - has blanks cutter

coaxial with induction heating furnace and horizontal press

INVENTOR: BREITBURD, A M; KUKUSHKIN, V A; LAPIN YU, V

PRIORITY-DATA: 1989SU-4772923 (December 22, 1989)

PATENT-FAMILY:

PUB-NO PUB-DATE

LANGUAGE

PAGES MAIN-IPC

SU 1731336 A1

May 7, 1992

004

B21C023/00

INT-CL (IPC): B21C 23/00

☐ 2. Document ID: WO 8701375 A, FR 2586428 A, EP 235187 A, PT 83255 A, DK 8702089 A, JP 63500662 W, ES 2003339 A, CA 1279276 C, EP 235187 B, DE 3682893 G, JP

Full Title Citation Front Review Classification Date Reference

08308597 A, JP 2755574 B2, JP 10114677 A, JP 2818745 B2, JP 11023577 A, US 5885770 A, DK 172647 B, US 5919615 A, US 5955260 A, US 6010704 A, JP 3067734 B2, JP 3294787 B2

L14: Entry 2 of 3

File: DWPI

Mar 12, 1987

Claims KWIC Draw, De

DERWENT-ACC-NO: 1987-079685

DERWENT-WEEK: 200245

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TITLE: Kit contg. polypeptide(s) expressed by several Gps. of papilloma virus - and similar kits contg. derived antibodies, useful in vaccines, diagnosis and treatment

INVENTOR: BREITBURD, F; CROISSANT, O; KOMLY, C A

PRIORITY-DATA: 1985FR-0012750 (August 26, 1985), 1995US-0466693 (June 6, 1995)

PATENT-FAMILY:

PUB-NO PUB-DATE LANGUAGE PAGES MAIN-IPC

<u>WO 8701375 A</u> March 12, 1987 F 073 <u>FR 2586428 A</u> February 27, 1987 000 Record List Display Page 2 of 3

EP 235187 A	September 9, 1987	F	000	
PT 83255 A	September 30, 1987		000	
DK 8702089 A	June 26, 1987		000	
JP 63500662 W	March 10, 1988		000	
ES 2003339 A	November 1, 1988		000	
CA 1279276 C	January 22, 1991		000	
EP 235187 B	December 11, 1991		000	
DE 3682893 G	January 23, 1992		000	
JP 08308597 A	November 26, 1996		026	C12Q001/68
JP 2755574 B2	May 20, 1998		027	A61K039/12
JP 10114677 A	May 6, 1998		024	A61K039/12
JP 2818745 B2	October 30, 1998		027	G01N033/569
JP 11023577 A	January 29, 1999		021	G01N033/569
US 5885770 A	March 23, 1999		000	C12Q001/70
DK 172647 B	April 6, 1999		000	C07K014/025
US 5919615 A	July 6, 1999 '		000	C12Q001/70
<u>US 5955260 A</u>	September 21, 1999		000	C12Q001/70
US 6010704 A	January 4, 2000		000	A61K039/12
JP 3067734 B2	July 24, 2000		021	G01N033/569
JP 3294787 B2	June 24, 2002		025	C12Q001/68

172647 B INT-CL (IPC): A61K 39/12; A61K 39/395; C07H 21/04; C07K 14/025; C07K 15/00; C07K 16/08; C12N 15/00; C12N 15/09; C12P 21/00; C12P 21/06; C12P 21/08; C12Q 1/02; C12Q 1/68; C12Q 1/70; G01N 33/56; G01N 33/569; G01N 33/574; C12P 21/00; C12R 1/19; C12N 15/09; C12R 1/92; C12P 21/00; C12R 1/19; C12P 21/00; C12R 1/19; C12P 21/00; C12R 1/19

Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	KWIC	Draw, De

### ☐ 3. Document ID: EP 174228 A, FR 2568682 A, JP 61070465 A

L14: Entry 3 of 3

File: DWPI

Mar 12, 1986

DERWENT-ACC-NO: 1986-070722

DERWENT-WEEK: 198611

COPYRIGHT 2004 DERWENT INFORMATION LTD

TITLE: Diagnostic detection of human papilloma virus - by immune reaction with

monoclonal antibody specific for a single virus type

INVENTOR: BREITBURD, F; GUILLEMIN, M C; ORTH, G; PERIES, G; POTHIER, P; ROSETO,

Α

PRIORITY-DATA: 1984FR-0012226 (August 1, 1984)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES MAIN-I	PC
EP 174228 A	March 12, 1986	F	017	
FR 2568682 A	February 7, 1986		000	
JP 61070465 A	April 11, 1986		000	

Record List Display Page 3 of 3

INT-CL (IPC): A61K 39/39; C07K 15/00; C12N 5/00; C12N 7/00; C12N 15/00; C12P 21/00; G01N 33/56

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KWAC	Draw, De
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Search Results - Record(s) 1 through 10 of 45 returned.

☐ 1. Document ID: US 6734173 B1

L23: Entry 1 of 45 File: USPT May 11, 2004

US-PAT-NO: 6734173

DOCUMENT-IDENTIFIER: US 6734173 B1

TITLE: HSP DNA vaccines

DATE-ISSUED: May 11, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Wu; Tzyy-Choou Stevenson MD Hung; Chien-Fu Brookeville MD

US-CL-CURRENT: <u>514/44</u>; <u>536/23.5</u>

Full Title Citation Front Review Classification Date Reference

☐ 2. Document ID: US 6723317 B2

L23: Entry 2 of 45 File: USPT Apr 20, 2004

US-PAT-NO: 6723317

DOCUMENT-IDENTIFIER: US 6723317 B2

TITLE: Antibodies specific for seroreactive regions on HPV 16 protein E1

DATE-ISSUED: April 20, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Muller; Martin Heidelberg `DE Gissmann; Lutz Wiesloch DE

US-CL-CURRENT: 424/130.1; 424/186.1, 424/204.1, 435/345, 435/7.9, 530/300

Full Title Citation Front Review Classification Date Reference Continued State Chaires KMC Draw, De

☐ 3. Document ID: US 6657055 B2

L23: Entry 3 of 45

File: USPT

Dec 2, 2003

US-PAT-NO: 6657055

DOCUMENT-IDENTIFIER: US 6657055 B2

\*\* See image for Certificate of Correction \*\*

TITLE: Induction of a Th1-like response in vitro

DATE-ISSUED: December 2, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Siegel; Marvin Blue Bell PA

Chu; N. Randall Victoria CA Mizzen; Lee A. Victoria CA

US-CL-CURRENT: 536/23.72; 435/69.7

Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	KWIC	Draw, De

☐ 4. Document ID: US 6605281 B1

L23: Entry 4 of 45 File: USPT

Aug 12, 2003

US-PAT-NO: 6605281

DOCUMENT-IDENTIFIER: US 6605281 B1

TITLE: Human papillomavirus vectors for the episomal transduction of host cells and

method of making same

DATE-ISSUED: August 12, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Broker; Thomas R. Mountain Brook AL Chow; Louise T. Mountain Brook AL Sorscher; Eric J. Birmingham AL Zou; Nianxiang Homewood AL Gadi; Vijayakrishna K. Birmingham AL

US-CL-CURRENT: 424/199.1; 424/204.1, 435/235.1, 435/252.3, 435/320.1, 435/325,

<u>435/69.1</u>, <u>536/23.1</u>, <u>536/23.72</u>

Full	Title Citation	Front R	Review C	lassification	Date	Reference		Claims	KWC	Draw, De
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	5. Docum	ent ID: U	J <b>S</b> 6599	9508 B1						
L23:	Entry 5 of	45				File: U	SPT	Jul	29,	2003

Record List Display Page 3 of 5

US-PAT-NO: 6599508

DOCUMENT-IDENTIFIER: US 6599508 B1

TITLE: Papilloma virus-like particles, fusion proteins as well as processes for

their production

DATE-ISSUED: July 29, 2003

INVENTOR-INFORMATION:

ZIP CODE COUNTRY CITY STATE NAME

Gissmann; Lutz Willowbrook ILILZhou; Jian Willowbrook Muller; Martin Chicago ILPainstil; Jeanette Westchester IL

US-CL-CURRENT: 424/204.1; 424/184.1, 424/186.1, 424/205.1, 435/69.1, 435/69.3,

536/23.72

Full Title Citation Front Review Classification Date Reference Claims 1000C Draw, De ☐ 6. Document ID: US 6531127 B2 L23: Entry 6 of 45 File: USPT Mar 11, 2003

US-PAT-NO: 6531127

DOCUMENT-IDENTIFIER: US 6531127 B2

TITLE: Antibodies that specifically react with seroreactive regions on HPV 16

proteins E1 and E2

DATE-ISSUED: March 11, 2003

INVENTOR-INFORMATION:

STATE ZIP CODE COUNTRY NAME CITY

Muller; Martin DE Heidelberg DE Gissmann; Lutz Wiesloch

US-CL-CURRENT: 424/130.1; 424/147.1, 424/159.1, 424/186.1, 424/204.1, 435/345,

435/5, 435/7.9, 435/7.91, 530/300

Full Title Citation Front Review Classification Date Reference 7. Document ID: US 6500641 B1 L23: Entry 7 of 45 File: USPT Dec 31, 2002

US-PAT-NO: 6500641

DOCUMENT-IDENTIFIER: US 6500641 B1

TITLE: Compositions and methods for identifying antigens which elicit an immune

response

Record List Display Page 4 of 5

DATE-ISSUED: December 31, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Chen; Si-Yi Pearland TX You; Zhaoyang Houston TX

US-CL-CURRENT: 435/69.1; 424/159.1, 435/6, 530/387.3, 530/388.3

Full Title Citation Front Review Classification Date Reference With Communication Date Reference With Commun

US-PAT-NO: 6485728

DOCUMENT-IDENTIFIER: US 6485728 B2

TITLE: Formalin-Inactivated human papillomavirus L1 protein vaccine

DATE-ISSUED: November 26, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Schlegel; C. Richard Rockville MD
Jenson; A. Bennett Rockville MD
Ghim; Shin-je Washington DC

US-CL-CURRENT: 424/204.1; 424/184.1, 424/186.1, 424/199.1, 536/23.72

Full Title Citation Front Review Classific	cation Date Reference	Claims KWMC Draw, De
***************************************		
☐ 9. Document ID: US 6482588	B1	
L23: Entry 9 of 45	File: USPT	Nov 19, 2002

US-PAT-NO: 6482588

DOCUMENT-IDENTIFIER: US 6482588 B1

TITLE: Detection and identification of human papillomavirus by PCR and type-

specific reverse hybridization

DATE-ISSUED: November 19, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Van Doorn; Leen-Jan Ridderkerk NL
Quint; Wim Nootdorp NL

Kleter; Berhnard Delft NL TerSchegget; Jan Amsterdam NL Record List Display Page 5 of 5

US-CL-CURRENT: 435/5; 435/6, 435/91.1, 536/24.32

Full Title Citation Front Review Classification Date Reference State State State Claims KWC Draw. Co

File: USPT

US-PAT-NO: 6478749

L23: Entry 10 of 45

DOCUMENT-IDENTIFIER: US 6478749 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Diagnostic kit for skin tests, and method

DATE-ISSUED: November 12, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Nov 12, 2002

Hopfl; Reinhard

Innsbruch

AT

US-CL-CURRENT: 600/556; 206/569

Full T	itle   Citation   Front   Review   Classification   Da	ste Reference	Claims KWC Draw. [•
Clear	Generate Collection Print	Fwd Refs Bkwd Refs	Generate OACS
	Terms	Documents	
	E6 and HPV 16.clm.		45

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